

**REMARKS**

The Office Action of October 22, 2002, and the cited and applied references have been carefully reviewed. Claims 7 and 18 are cancelled. Claims 8-12 and 14-15 are allowed. Claims 2-6, 8-17 and 19-24 presently appear in the application and define patentable subject matter warranting their allowance. Accordingly, applicants respectfully request favorable consideration and allowance.

Claim 6 is objected to because of an informality, the misspelling of the word "metastasis". Said informality has been corrected.

Claim 18 is objected to because of an informality and has been canceled.

Claims 2-7, 13, and 16-18 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. This rejection is respectfully traversed.

The Examiner states that claim 6 is vague and indefinite in the recitation of "diagnosed correctly". Applicants have amended the claim and stricken "correctly" therefrom.

The Examiner states that claims 6 and 16 are vague and indefinite in the recitation "crossover index or the ratio". Claims 6 and 16 have been amended to eliminate the objected to language.

The Examiner further states that claims 6, 7, 16 and 17 are vague and indefinite in their description of the "crossover index" and "ratio". Claim 7 has been canceled and claims 6, 16 and 17 have been amended to improve their form.

Finally, the Examiner states that claim 13 is vague and indefinite for the recitation of osteocalcin. In this claim, those markers of bone formation that appear at different phases are used. Claim 13 states the following two kinds of combinations of markers: 1) PICP or PINP, in the phase of proliferation and osteocalcin in the phase of calcification and 2) BALP in the phase of matrix formation and osteocalcin, in the phase of calcification. Osteocalcin is therefore used as a necessary marker in each of the above combinations, wherein each kind of bone formation marker is directed to different phases.

Osteocalcin, a noncollagenous bone protein synthesized by the osteoblast, has been suggested as a good biochemical marker for bone turnover or bone formation. It is the most specific marker for the mature osteoblastic phenotype (not osteoclasts, as the rejection suggests, see, e.g., Duarte

et al. 18 J. Bone Miner. Res. 493 (2003), the abstract of which is attached) and as such is a bone formation marker, see the Table 1 on page 2 of the instant specification.

For these reasons, reconsideration and withdrawal of the rejection are respectfully requested.


As there are no rejections based on prior art, applicants understand that all of applicants' claims are deemed by the PTO to define novel and unobvious subject matter under Sections 102 and 103.

In view of the above, the claims comply with 35 USC §112 and define patentable subject matter warranting their allowance. Favorable consideration and allowance are respectfully urged.

Respectfully submitted,

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